EXPLORATORY/DEVELOPMENTAL (R21) BIOENGINEERING RESEARCH GRANTS (EBRG)

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National Cancer Institute (NCI)
(http://www.nci.nih.gov)
National Center for Research Resources (NCRR)
(http://www.ncrr.nih.gov)
National Eye Institute (NEI)
(http://www.nei.nih.gov)
National Heart, Lung, and Blood Institute (NHLBI)
(http://www.nhlbi.nih.gov)
National Human Genome Research Institute (NHGRI)
(http://www.nhgri.nih.gov)
National Institute on Aging (NIA)
(http://www.nia.nih.gov)
National Institute on Alcohol Abuse and Alcoholism (NIAAA)
(http://www.niaaa.nih.gov)
National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS)
(http://www.niams.nih.gov)
National Institute of Biomedical Imaging and Bioengineering (NIBIB)
(http://www.nibib.nih.gov)
National Institute on Drug Abuse (NIDA)
(http://www.nida.nih.gov)
National Institute on Deafness and Other Communication Disorders (NIDCD)
(http://www.nidcd.nih.gov)
National Institute of Dental and Craniofacial Research (NIDCR)
(http://www.nidcr.nih.gov)
National Institute of Environmental Health Sciences (NIEHS)
(http://www.niehs.nih.gov)
National Institute of General Medical Sciences (NIGMS)
(http://www.nigms.nih.gov)
National Institute of Mental Health (NIMH)

(http://www.nimh.nih.gov)
National Institute of Neurological Disorders and Stroke (NINDS)
(http://www.ninds.nih.gov)

THIS PA CONTAINS THE FOLLOWING INFORMATION

PURPOSE OF THIS PA

Participating Institutes and Centers (ICs) of the National Institutes of Health (NIH) invite applications for Exploratory/Developmental Bioengineering Research Grants (EBRG) to support innovative, high risk/high impact bioengineering research in new areas that are lacking preliminary testing or development. This research can explore approaches and concepts new to a particular substantive area; research and development of new technologies, techniques or methods; or initial research and development of data upon which significant future research may be built.

While this program announcement (PA) is intended to encourage innovation and high impact research, and while minimal preliminary data are expected to be described in the application, applications should clearly indicate the significance of the proposed work and that the proposed research and/or development is scientifically sound, that the qualifications of the investigators are appropriate, and that resources available to the investigators are adequate.

RESEARCH OBJECTIVES

The objective of this PA is to invite applications in exploratory or developmental bioengineering research (EBRG). The EBRG can support: 1) innovative, high-risk research, for which preliminary results have not yet been obtained; 2) exploration of new approaches or concepts to a particular substantive area; 3) research and development of new technologies, techniques or methods; or 4) initial research and development of data upon which significant future research may be built.

The EBRG will support exploratory or developmental bioengineering research that is not appropriate for the R01 grant mechanism. While the core review criteria of 'significance', 'approach', 'innovation', 'investigator', and 'facilities' are retained, the balance between risk, benefit, and the cost of the research is shifted toward accepting a significant risk of failure for a potential great benefit. The EBRG is appropriate for early stages of research or for investigating new ideas where risk is high but potential significance is also high and where the research needed to make a decision about proceeding to a larger scale R01 effort is moderate in terms of time and money. A simple scenario would be a situation in which an investigator studying gene delivery conceives of a completely new, but unproven way to deliver genes. If the justification for the idea is solid, the feasibility of the idea can be effectively evaluated (with the EBRG), and if the potential significance is high then the feasibility could be supported in the absence of extensive preliminary results.

Areas of Bioengineering Research for an EBRG

Bioengineering is defined as follows: Bioengineering integrates physical, chemical, or mathematical sciences and engineering principles for the study of biology, medicine, behavior, or health. It advances fundamental concepts, creates knowledge from the molecular to the organ systems level, and develops innovative biologics, materials, processes, implants, devices, and informatics approaches for the prevention, diagnosis, and treatment of disease, for patient rehabilitation, and for improving health. A few examples of bioengineering areas of relevance to the mission of Institutes and Centers (ICs) are identified below. This list is illustrative only; it is not intended to be exclusive.

Examples of Bioengineering Research:

o Development of molecular probes for imaging of structure or function
o Development of new imaging modalities
o Development of organ culture systems
o Development of biomaterials or engineered tissues

o Development or evaluation of prostheses
o Development of medical implants, biomembranes, or sensors
o Development of tools for robotic or non-invasive surgery
o Development of microarrays or other tools for genomics
o Development of combinatorial or other techniques for high-throughput screening
o Development of techniques for bioprocessing
o Research on the biomechanics of tissue injury or repair, and standing or walking
o Research on the interactions between biomaterials and living systems
o Research on drug, gene, or cellular therapeutic delivery systems
o Research on the interaction of magnetic or other fields with biological systems

MECHANISM OF SUPPORT

This PA will use the NIH R21 award mechanism. As an applicant, you will be solely responsible for planning, directing, and executing the proposed project. Under this program announcement, applicants for the EBRG award may request direct costs of up to $275,000 distributed over two years. The EBRGs are in addition to a related program announcement (PA) PA-02-011 for Bioengineering Research Grants [(BRGs) http://grants.nih.gov//grants/guide/pa-files/PA-02-011.html]. The BRGs differ from the EBRGs in that the BRG utilizes the R01 grant mechanism and requires strong preliminary data for hypothesis-driven, discovery-driven, developmental, or design-directed research. The EBRG cannot be renewed; if sufficient results are generated during the term of the award, investigators are encouraged to apply for further funding through the Bioengineering Research Grant (BRG) R01 mechanism.

This PA uses just-in-time concepts. It also uses the modular budgeting format. (see http://grants.nih.gov/grants/funding/modular/modular.htm). Specifically, if you are submitting an application with direct costs in each year of $250,000 or less, use the modular format.

ELIGIBLE INSTITUTIONS

You may submit (an) application(s) if your institution has any of the following characteristics:

o For-profit or non-profit organizations
o Public or private institutions, such as universities, colleges, hospitals, and laboratories
o Units of State and local governments
o Eligible agencies of the Federal government
o Domestic or foreign

o Faith-based or community-based organizations

INDIVIDUALS ELIGIBLE TO BECOME PRINCIPAL INVESTIGATORS

Any individual with the skills, knowledge, and resources necessary to carry out the proposed research is invited to work with their institution to develop an application for support. Individuals from underrepresented racial and ethnic groups as well as individuals with disabilities are always encouraged to apply for NIH programs.

WHERE TO SEND INQUIRIES

We encourage your inquiries concerning this PA and welcome the opportunity to answer questions from potential applicants. Inquiries may fall into three areas: scientific/research, peer review, and financial or grants management issues:

o NIH BECON scientific and financial contacts listed at the following Web site should be contacted for answers to questions about scientific or financial issues:

http://www.becon.nih.gov/becon_contacts.htm.

o Direct your questions about peer review issues to:

Dr. Eileen Bradley
Center for Scientific Review
6701 Rockledge Drive
Bethesda, MD 20892
TEL: 301-435-1179
FAX: 301-480-2241
E-mail: bradleye@csr.nih.gov

SUBMITTING AN APPLICATION

Applications must be prepared using the PHS 398 research grant application instructions and forms (rev. 5/2001). The PHS 398 is available at http://grants.nih.gov/grants/funding/phs398/phs398.html in an interactive format. For further assistance contact GrantsInfo, Telephone (301) 435-0714, Email: GrantsInfo@nih.gov.

APPLICATION RECEIPT DATES: Applications submitted in response to this program announcement will be accepted at the standard application deadlines, which are available at http://grants.nih.gov/grants/dates.htm. Application deadlines are also indicated in the PHS 398 application kit.

SPECIFIC INSTRUCTIONS FOR MODULAR GRANT APPLICATIONS: Applications requesting up to $250,000 per year in direct costs must be submitted in a modular grant format. The modular grant format simplifies the preparation of the budget in these applications by limiting the level of budgetary detail. Applicants request direct costs in $25,000 modules. Section C of the research grant application instructions for the PHS 398 (rev. 5/2001) at http://grants.nih.gov/grants/funding/phs398/phs398.html includes step-by-step guidance for preparing modular grants. Additional information on modular grants is available at http://grants.nih.gov/grants/funding/modular/modular.htm.

All PHS 398 requirements should be followed, with the exception of those items affected by the following instructions. Applications not conforming to the requested format will be returned to the applicant without review

o FACE PAGE- Item 2, Check the box marked "Yes" and type the number and title (EXPLORATORY/DEVELOPMENTAL (R21) BIOENGINEERING RESEARCH GRANTS) of this program announcement.

o Item 6: Up to a total of two years of support may be requested.

o RESEARCH PLAN- Do not exceed a total of 15 pages inclusive of the following sections: Specific Aims; Background and Significance; Preliminary Studies/Progress Report (evidence of feasibility); and Research Design and Methods. Tables, figures and photographs are included in the 15-page limitation.

o Item a, SPECIFIC AIMS- The applicant should begin with a statement that justifies the designation of the application as an Exploratory/Developmental Research Grant as defined under the PURPOSE section of this program announcement.

o Item b, BACKGROUND AND SIGNIFICANCE- In this section it is important to provide enough information to give the reviewers an understanding of the potential significance of this work and to identify clearly how the application addresses the specific objectives of this program announcement. Briefly review the relevant state-of-the-art, and concisely describe the substantial

advance beyond state-of-the-art that would be achieved if the project is successful. Indicate how this advance might impact on human health. For innovations that involve multiple steps justify that the proposed research will investigate the highest-risk critical step of the process. Identify briefly how this application relates to the purpose of the R21 mechanism as stated in this program announcement (i.e., highly innovative, high risk/high impact research; exploration of the use of approaches and concepts new to a particular substantive area; research and development of new technologies, techniques or methods; or initial research and development of a body of data upon which significant future research may be built).

o Item c, PRELIMINARY STUDIES/PROGRESS REPORT- Minimal preliminary data are expected for an Exploratory/Developmental Grant application. However, if data are available they can be included in this section. Particularly in the absence of preliminary data, describe the theoretical or conceptual underpinnings of the proposed project. If substantial preliminary data are available the investigator should consider submitting a BRG application.

o Item d, RESEARCH DESIGN AND METHODS- Fully describe the research design and methods. In many cases, an Exploratory/Developmental Grant mechanism will support novel research in an area or the research and development of new technologies. Where appropriate, specific criteria by which to judge the feasibility of novel approaches (including milestones that will mark progress) should be explicitly described in this section. Milestones should be as quantitative as possible. Identify the key technical challenges and propose highest priority alternative solutions.

o APPENDIX– Publications may not be submitted, but color/glossy photographs and other appendix material (surveys, questionnaires, etc.) is permitted.

SENDING AN APPLICATION TO THE NIH: Submit a signed, typewritten original of the application, including the checklist, and five signed photocopies in one package to:

Center for Scientific Review
National Institutes of Health
6701 Rockledge Drive, Room 1040, MSC 7710
Bethesda, MD 20892-7710
Bethesda, MD 20817 (for express/courier service)

APPLICATION PROCESSING: Applications must be received by or mailed on or before the receipt dates described at http://grants.nih.gov/grants/funding/submissionschedule.htm. The CSR

will not accept any application in response to this PA that is essentially the same as one currently pending initial review unless the applicant withdraws the pending application. The CSR will not accept any application that is essentially the same as one already reviewed. This does not preclude the submission of a substantial revision of an application already reviewed, but such application must include an Introduction addressing the previous critique.

PEER REVIEW PROCESS

Applications submitted for this PA will be assigned on the basis of established PHS referral guidelines. An appropriate scientific review group that includes bioengineering expertise will evaluate applications for scientific and technical merit convened in accordance with NIH peer review procedures (http://www.csr.nih.gov/refrev.htm).

As part of the initial merit review, all applications will:

o Receive a written critique
o Undergo a selection process in which only those applications deemed to have the highest scientific merit, generally the top half of applications under review, will be discussed and assigned a priority score
o Receive a second level review by the appropriate national advisory council or board

REVIEW CRITERIA

The goals of NIH-supported research are to advance our understanding of biological systems, improve the control of disease, and enhance health. In the written comments, reviewers will be asked to discuss the following aspects of your application in order to judge the likelihood that the proposed research will have a substantial impact on the pursuit of these goals:

o Significance
o Approach
o Innovation
o Investigator
o Environment

These NIH review criteria have been expanded to reflect the exploratory and bioengineering focus of an EBRG application. The score should reflect the overall impact that the EBRG award could have on the selected area of bioengineering research based on consideration of the five

criteria, with the emphasis on each criterion varying from one application to another, depending on the nature of the application and its relative strengths. Note that an application need not be strong in all categories to be judged likely to have major scientific impact and thus deserve a high priority score. The review criteria are:

(1) Significance. If the Specific Aims of the EBRG are achieved, will they provide significant advances in the selected area of bioengineering research? Is the research likely to provide a foundation for a new research area or have potential for wide applicability? Does this represent a groundbreaking, precedent setting research topic that clearly requires additional preliminary data for its potential to be assessed?

(2) Approach. Are the EBRG approaches and methods adequately developed, well integrated, and appropriate to the aims of the project? Does the applicant acknowledge potential problem areas and consider alternative tactics? For technology development projects, are the milestones sufficiently specific and quantitative to guide both the research and subsequent evaluation of success or failure of the proposed concept?

(3) Innovation. Does the EBRG propose new approaches or explore new research paradigms or new concepts that will affect bioengineering, basic or clinical sciences? Are extant approaches or concepts applied to new scientific problems in novel ways?

(4) Investigators. Are the PI and key personnel appropriately trained in their disciplines and capable of conducting the proposed research?

(5) Environment. Does the scientific and technological environment in which the work will be done contribute to the probability of success? Does the proposed research take advantage of unique features of the scientific environment or employ useful collaborative arrangements? Is there evidence of other support that will contribute to the success of the research?

ADDITIONAL REVIEW CRITERIA: In addition to the above criteria, your application will also be reviewed with respect to the following:

PROTECTIONS: The adequacy of the proposed protection for humans, animals, or the environment, to the extent they may be adversely affected by the project proposed in the application.

INCLUSION: The adequacy of plans to include subjects from both genders, all racial and ethnic groups (and subgroups), and children as appropriate for the scientific goals of the research. Plans for the recruitment and retention of subjects will also be evaluated. (See Inclusion Criteria included in the section on Federal Citations, below)

BUDGET: The reasonableness of the proposed budget and the requested period of support in relation to the proposed research.

AWARD CRITERIA

Applications submitted in response to a PA will compete for available funds with all other recommended applications. The following will be considered in making funding decisions:

o Scientific merit of the proposed project as determined by peer review
o Availability of funds
o Relevance to program priorities

REQUIRED FEDERAL CITATIONS

MONITORING PLAN AND DATA SAFETY AND MONITORING BOARD: Research components involving Phase I and II clinical trials must include provisions for assessment of patient eligibility and status, rigorous data management, quality assurance, and auditing procedures. In addition, it is NIH policy that all clinical trials require data and safety monitoring, with the method and degree of monitoring being commensurate with the risks (NIH Policy for Data Safety and Monitoring, NIH Guide for Grants and Contracts, June 12, 1998: http://grants.nih.gov/grants/guide/notice-files/not98-084.html).

INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH: It is the policy of the NIH that women and members of minority groups and their sub-populations must be included in all NIH-supported clinical research projects unless a clear and compelling justification is provided indicating that inclusion is inappropriate with respect to the health of the subjects or the purpose of the research. This policy results from the NIH Revitalization Act of 1993 (Section 492B of Public Law 103-43).

All investigators proposing clinical research should read the AMENDMENT "NIH Guidelines for Inclusion of Women and Minorities as Subjects in Clinical Research - Amended, October, 2001," published in the NIH Guide for Grants and Contracts on October 9, 2001

(http://grants.nih.gov/grants/guide/notice-files/NOT-OD-02-001.html); a complete copy of the updated Guidelines are available at http://grants.nih.gov/grants/funding/women_min/guidelines_amended_10_2001.htm. The amended policy incorporates: the use of an NIH definition of clinical research; updated racial and ethnic categories in compliance with the new OMB standards; clarification of language governing NIH-defined Phase III clinical trials consistent with the new PHS Form 398; and updated roles and responsibilities of NIH staff and the extramural community. The policy continues to require for all NIH-defined Phase III clinical trials that: a) all applications or proposals and/or protocols must provide a description of plans to conduct analyses, as appropriate, to address differences by sex/gender and/or racial/ethnic groups, including subgroups if applicable; and b) investigators must report annual accrual and progress in conducting analyses, as appropriate, by sex/gender and/or racial/ethnic group differences.

INCLUSION OF CHILDREN AS PARTICIPANTS IN RESEARCH INVOLVING HUMAN SUBJECTS: The NIH maintains a policy that children (i.e., individuals under the age of 21) must be included in all human subjects research, conducted or supported by the NIH, unless there are scientific and ethical reasons not to include them. This policy applies to all initial (Type 1) applications submitted for receipt dates after October 1, 1998.

All investigators proposing research involving human subjects should read the "NIH Policy and Guidelines" on the inclusion of children as participants in research involving human subjects that is available at http://grants.nih.gov/grants/funding/children/children.htm.

REQUIRED EDUCATION ON THE PROTECTION OF HUMAN SUBJECT PARTICIPANTS: NIH policy requires education on the protection of human subject participants for all investigators submitting NIH proposals for research involving human subjects. You will find this policy announcement in the NIH Guide for Grants and Contracts Announcement, dated June 5, 2000, at http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-039.html.

HUMAN EMBRYONIC STEM CELLS (hESC): Criteria for federal funding of research on hESCs can be found at http://grants.nih.gov/grants/stem_cells.htm and at http://grants.nih.gov/grants/guide/notice-files/NOT-OD-02-005.html.
Only research using hESC lines that are registered in the NIH Human Embryonic Stem Cell Registry will be eligible for Federal funding (see http://escr.nih.gov). It is the responsibility of the applicant to provide the official NIH identifier(s)for the hESC line(s) to be used in the proposed research. Applications that do not provide this information will be returned without review.

PUBLIC ACCESS TO RESEARCH DATA THROUGH THE FREEDOM OF INFORMATION ACT: The Office of Management and Budget (OMB) Circular A-110 has been revised to provide public access to research data through the Freedom of Information Act (FOIA) under some circumstances. Data that are (1) first produced in a project that is supported in whole or in part with Federal funds and (2) cited publicly and officially by a Federal agency in support of an action that has the force and effect of law (i.e., a regulation) may be accessed through FOIA. It is important for applicants to understand the basic scope of this amendment. NIH has provided guidance at http://grants.nih.gov/grants/policy/a110/a110_guidance_dec1999.htm.

Applicants may wish to place data collected under this PA in a public archive, which can provide protections for the data and manage the distribution for an indefinite period of time. If so, the application should include a description of the archiving plan in the study design and include information about this in the budget justification section of the application. In addition, applicants should think about how to structure informed consent statements and other human subjects procedures given the potential for wider use of data collected under this award.

URLs IN NIH GRANT APPLICATIONS OR APPENDICES: All applications and proposals for NIH funding must be self-contained within specified page limitations. Unless otherwise specified in an NIH solicitation, Internet addresses (URLs) should not be used to provide information necessary to the review because reviewers are under no obligation to view the Internet sites. Furthermore, we caution reviewers that their anonymity may be compromised when they directly access an Internet site.

HEALTHY PEOPLE 2010: The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2010," a PHS-led national activity for setting priority areas. This PA is related to one or more of the priority areas. Potential applicants may obtain a copy of "Healthy People 2010" at http://www.health.gov/healthypeople.

AUTHORITY AND REGULATIONS: This program is described in the Catalog of Federal Domestic Assistance Nos. 93.286, 93.287, 93.394, 93.395, 93.396, 93.306, 93.867, 93.172, 93.837, 93.838, 93.839, 93.866, 93.273, 93.855, 93.856, 93.846, 93.864, 93.865, 93.929, 93.279, 93.173, 93.121, 93.847, 93.848, 93.849, 93.113, 93.821, 93.859, 93.862, 93.242, 93.853, 93.361, and 93.879. Awards are made under authorization of Sections 301 and 405 of the Public Health Service Act as amended (42 USC 241 and 284) and administered under NIH grants policies described at http://grants.nih.gov/grants/policy/policy.htm and Federal Regulations 42 CFR 52 and 45 CFR Parts 74 and 92. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

The PHS strongly encourages all grant recipients to provide a smoke-free workplace and discourage the use of all tobacco products. In addition, Public Law 103-227, the Pro-Children Act of 1994, prohibits smoking in certain facilities (or in some cases, any portion of a facility) in which regular or routine education, library, day care, health care, or early childhood development services are provided to children. This is consistent with the PHS mission to protect and advance the physical and mental health of the American people.

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Department of Health
and Human Services


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